

# ISPE–EURODURG 2014

Conference Report

27-29 August 2014  
Groningen, The Netherlands

**EURODURG 2014**

DRUG UTILISATION RESEARCH:  
SUPPORTING RATIONAL DRUG  
USE FOR PUBLIC HEALTH AND  
INDIVIDUAL PATIENT CARE



**EuroDURG**, the European Drug Utilization Research Group, is a multidisciplinary scientific non-profit organization with the aim to promote drug utilization research as a means of improving the quality use of medicines. This is achieved by providing an international forum for communication and cooperation between academic researchers, healthcare professionals, regulatory agencies and other stakeholders interested in drug utilization research.

EuroDURG is the European Chapter of the Drug Utilization Research Special Interest Group of the International Society for Pharmacoepidemiology (ISPE).

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## Executive summary

Held on 27–29 August, 2014, at the University Medical Center Groningen (Groningen, the Netherlands), the ISPE–EuroDURG 2014 conference jointly organized by the European branch of ISPE SIG-DUR (EuroDURG) and the University of Groningen, was a successful event that brought together over 300 participants representing academia, healthcare providers, regulatory agencies, payers and policy makers from 40 countries.

The meeting opened with a plenary session on *Europe's Role in the Globalization of Drug Utilization Research* with keynote speakers Aukje Mantel-Teeuwisse and Björn Wettermark discussing present challenges in drug therapy and innovation and potential solutions for the future. The closing plenary session logically focused on the *Challenges and Opportunities for Future Drug Utilization Research* and offered keynote lectures on the perspectives of policy makers (Bert Leufkens), healthcare providers (Frank May) and patients (Nicky Britten).

A great variety of papers (32 oral and over 250 poster presentations) addressing various aspects of drug utilization research was presented. These papers were divided into the following sessions: Adherence to Medication, Drug Utilization as a Tool for Health Policy, Drug Use in Hospitals, Comparison of Drug Use across Nations, Trend and Cohort Studies, Drug Utilization in Older Adults, Drug Utilization in Children and Pregnant Women, Drug Utilization and Pharmacovigilance. The number of research questions highlighted the eclectic nature of drug utilization research and the strong links both with pharmacoepidemiology and health services research.

The meeting also included three workshops. In the *Evaluating Impact of Interventions* workshop, participants were asked to design an intervention study to evaluate impact of a national policy, using the case of regulatory warnings. The *Patient Perspective on Adverse Drug Reactions* workshop focused on patients' role in identifying adverse drug reactions; the workshop participants discussed questions around incorporating the patients' voice in medication safety decision-making. Finally, the *Drug Utilization Research in the Introduction of New Drugs* workshop included presentations from three countries (Italy, Spain, the Netherlands) that have implemented patient registries, conditional reimbursement schemes or physician incentive schemes for the utilization of new drugs. The presentations were followed by discussions around key criteria to consider when monitoring utilization patterns for new drugs post launch.

Prior to the conference, several educational sessions were held, covering methodology (Data Sources Including Quality and Validity, Classification Systems and Measurement Units of Drug Utilization, Methods for Assessing Drug Use and Outcomes in Longitudinal Databases, Statistical Methods for Multilevel and Longitudinal Analysis of Drug Utilization, Visualization of Drug Utilization Data) as well as applications (Measuring Patient Adherence, Prescribing Quality Indicators, Assessing and Explaining Variability in Drug Utilization) of drug utilization research.

The ISPE–EuroDURG 2014 also celebrated the remarkable career of Flora Haaijer-Ruskamp, Professor in Drug Utilisation Studies at the University of Groningen. The dedicated symposium included lectures from Robert Vander Stichele, Bert Leufkens, Niek Klazinga, Petra Denig and, of course, Flora herself showing the width and depth of her research during the years.



## Message from the organizers

We are pleased to provide you with this official report from the ISPE–EuroDURG 2014 conference in Groningen, the Netherlands. The conference, entitled *Drug Utilisation Research: Supporting Rational Drug Use for Public Health and Individual Patient Care*, was a success due to the large number of participants and the high quality scientific program including a wide range of topics related to prescribing, dispensing and use of medicines. A special highlight was the symposium to celebrate the career of Flora Haaijer-Ruskamp, Professor in Drug Utilisation Studies at the University of Groningen, and one of the key pioneers in the research field.

The meeting gathered more than 300 participants from 40 countries across the globe and was the largest EuroDURG conference held so far. The program was built upon years of knowledge drawn from previous conferences and consisted of interactive educational sessions, keynote lectures on hot topics and special sessions dedicated to some areas undergoing a rapid development in drug utilization research. These areas were also selected based on a survey distributed to active drug utilization researchers.

In this report, we give an overview of the scientific content, educational program, the submitted studies and the overall evaluation of the meeting. We hope that the report will revive some good memories for those of you who were there and inspire those of you who did not have the opportunity to attend. We also hope that the report can serve as a basis for the planning of future conferences in pharmacoepidemiology and drug utilization research. Finally, may it whet your appetite for taking part in future EuroDURG conferences!

Stockholm and Groningen  
April, 2015

Björn Wettermark

Chair of the Scientific  
Committee

Petra Denig

Chair of the Local Organizing  
Committee



## Acknowledgements

A thank you goes to the Scientific Committee (chaired by Björn Wettermark) and the Local Organizing Committee in Groningen (chaired by Petra Denig). The meeting was made possible by generous support from the University of Groningen, the Municipality of Groningen and the Province of Groningen (the Netherlands), the University of Antwerp (Belgium), the University of Bologna (Italy), Karolinska Institutet (Sweden), EuroDURG and the International Society for Pharmacoepidemiology (ISPE). The chairs would like to thank these organizations for their commitment to our work, as well as those organizations that granted time to committee members to organize and participate in the ISPE–EuroDURG 2014 conference.

Special thanks to Irene Eriksson (Sweden), writer and editor of this report, supported by committee members; Yeonyoung Cho (the Netherlands), the conference photographer; Angela Acosta (Colombia), Tatiana Borges Luz (Brazil), Thomas Cars, Elin Dahlén, Desirée Loikas, Sten Ronge, Åke Pehrsson (Sweden) who contributed to the report; Aniko Veg, Pia Bastholm Rahmner (Sweden) and Gisbert Selke (Germany) for help with the evaluation of the meeting; and to all those who supported the Local Organizing Committee before, during and after the conference.



Local Organizing Committee: Katja Taxis and Petra Denig



## Conference committees

### Scientific Committee

Björn Wettermark (chair)	Sweden
Anna Birna Almarsdottir	Denmark
Morten Andersen	Sweden
Begler Begovic	Bosnia and Herzegovina
Ria Benkő	Hungary
Petra Denig	Netherlands
Monique Elseviers	Belgium
Eric van Ganse	France
Brian Godman	United Kingdom
Katrin Janhsen	Germany
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Marion Bennie	United Kingdom
Peter Mol	Netherlands
Elisabetta Poluzzi	Italy
Lisa Pont	Australia
Katja Taxis	Netherlands
Robert Vander Stichele	Belgium
Vera Vlahović-Palčevski	Croatia

### Local Organizing Committee, the Netherlands

Petra Denig (chair)	Netherlands
Katja Taxis	Netherlands
Peter Mol	Netherlands

## Conference overview

Held on 27–29 August, 2014, at the University Medical Center Groningen (Groningen, the Netherlands), the ISPE–EuroDURG 2014 conference, jointly organized by the European branch of ISPE SIG-DUR (EuroDURG) and the University of Groningen, was the biggest EuroDURG meeting in almost 20 years of history of EuroDURG. It brought together more than 300 participants representing academia, healthcare providers, regulatory agencies, payers and policy makers from 40 countries. There were three days of stimulating talks, debate and discussion about the past, present and future of drug utilization research. It included a full day of educational sessions, two plenaries, eight scientific sessions, three workshops, an OECD lunch session, a World Health Organization (WHO) exhibition and interactive poster presentations.



**The conference venue**

Also a great social program was provided for. After a long day of educational sessions all attendees were invited for a reception at the Academy Building, the main building of the University of Groningen, where a welcome was given to all by Prof Sibbrand Poppema, president of the University of Groningen.



**Countries represented at the ISPE–EuroDURG 2014 conference**



#### Reception at the Academy Building

Dick de Zeeuw, head of clinical pharmacology, and Björn Wettermark, chair of EuroDURG, gave complementary speeches.

The rich social program also included an evening party at a historical venue that used to be a pudding factory decades ago.

A full conference agenda is outlined in Appendix 1. The agenda for Flora Haaijer-Ruskamp's farewell symposium is provided in Appendix 2. Summaries of the educational courses and the scientific program are provided in this report.



#### Social event at Puddingfabriek

## Summary of the educational sessions

Wednesday, 27 August, 2014, was dedicated to educational sessions, both basic and advanced, to suit the interests of new and experienced drug utilization researchers. A total of eight sessions were held. Björn Wettermark, in an introductory lecture, emphasized that drug utilization research, defined as *an eclectic collection of descriptive and analytical methods for the quantification, the understanding and the evaluation of the processes of prescribing, dispensing and consumption of medicines, and for the testing of interventions to enhance the quality of these processes*, requires knowledge of several scientific disciplines. Continued learning and collaboration are therefore fundamental in the field.

### Basic educational sessions

The basic educational sessions included lectures on data sources used in drug utilization research, classification systems and measurement units, visualization of drug utilization data as well as prescribing quality indicators.

### Data sources for drug utilization research

Chaired by Björn Wettermark, this session aimed to illustrate the value of different data sources

that can be used for drug utilization research, and provide an overview and examples of record linkage and validation studies.

Tatiana Borges Luz guided the audience through primary and secondary data sources used in drug utilization research. She explained what primary data are and suggested a number of practical steps to collect primary data of high quality. Further, Tatiana defined and provided examples of secondary data sources: administrative and clinical databases. She outlined the advantages and disadvantages of primary and secondary data and gave guidance on selecting an appropriate data source for drug utilization research.

Building on Tatiana's presentation, Irene Eriksson spoke about the levels of analyses in drug utilization studies – from aggregate level drug statistics to individual level descriptive and analytical studies and more elaborate pharmacoepidemiologic study designs – and gave examples of research questions that would require record linkage. Irene then provided an overview of record linkage methods followed by examples of in-depth analyses of drug utilization based



**Maria Rikala, Irene Eriksson, Björn Wettermark and Tatiana Borges Luz presenting at the educational session**

on linked data from various data sources. Irene emphasized that while linking data on patients and prescribers from secondary data sources can help explain observed drug utilization patterns, some questions may remain unanswered, thus requiring primary collection of additional information.

Maria Rikala concluded the session with a presentation on the *Validity of Register Data on Drug Exposures*. She provided examples of exposure misclassification and outlined common reasons for it, including patient non-adherence and the lack of information on some drugs in secondary data (e.g., non-reimbursed and over-the-counter drugs as well as drugs used in hospitals, free drug samples, borrowed drugs and drugs purchased in other

countries or over the Internet). Then, Maria explained that the degree of exposure misclassification is usually evaluated by performing a comparison between two data sources to measure exposure misclassification (validity, if one data source is considered superior, and agreement, if neither data source is superior) and provided a step-by-step example of assessing validity of a data source based on her own research (*Validity of the Finnish Prescription Register for Measuring Psychotropic Drug Exposures among Elderly Finns*).

#### **Classification systems and measurement units of drug utilization**

The session, aimed at giving an overview of classification systems

for medicinal products and describing the Anatomical Therapeutic Chemical (ATC) classification system and the unit of measurement (DDD), was chaired by Hanne Strom and comprised presentations by Hanne Strom, Hege Salvesen Blix, and Solveig Sakshaug.

Hanne Strom, in her presentation on *Classification Systems and Measurement Units of Utilization*, talked about the history of the WHO Collaborating Centre for Drug Statistics Methodology and its current work. Hanne then gave an overview of the classification systems focusing on ATC. She spoke about the history of ATC, described the ATC/DDD methodology, the general principles for ATC classification, alterations. She also presented other classification systems including the European Pharmaceutical Market Research Association (EphMRA) and the British National Formulary (BNF) codes as well as the American Hospital Formulary Service (AHFS) Pharmacologic-Therapeutic Classification.

Hege Salvesen Blix then spoke about the *Concept of the Defined Daily Dose*. Hege started her presentation by defining the purpose of the ATC/DDD system as a tool for drug utilization research in order to improve the quality of drug use, with one

component of this being the comparison of drug utilization. Hege explained that the DDD system is based on main indication, maintenance dose and administration form and also pointed out that DDDs for combination products represent an important challenge. Hege also explained the principles of DDD alterations and provided a number of alteration examples. She concluded her presentation by listing benefits and limitations of DDD as a measuring unit.

Solveig Sakshaug concluded the session with a talk about *Applications of ATC/DDD in Health Policy and Drug Utilisation*. Solveig gave examples of different units of measurement including cost and volume based units. She then explained the principles of the national implementation of ATC/DDD. Solveig also provided various examples of using ATC/DDD methodology in drug utilization studies, such as studying patterns of use and changes over time, evaluating impact of various interventions, evaluating drug utilization in relation to adverse drug reactions and assessing the appropriateness of drug use.

### **Prescribing quality indicators**

The aim of this session, chaired by Petra Denig, was to outline definitions, taxonomy, and

domains of Prescribing Quality Indicators (PQI) and to present past and present developments and practical examples on the use of PQI for different purposes.

Petra Denig opened the session by giving an *Overview of Concepts Underlying Quality Assessment and Types of Prescribing Quality Indicators*. She explained the distinction between implicit and explicit assessment of appropriateness of prescribing and outlined the three areas of concern: underprescribing, misprescribing and overprescribing. Petra also provided definitions and examples of the types of PQI (drug-oriented and disease-oriented) and

pointed out the importance of selecting the indicators that are appropriate and valid for the intended quality assessment.

Grigory Sidorenkov then spoke about the *Development and Validation of Prescribing Quality Indicators*. He explained the types of PQI validity (content validity – PQIs are selected/developed based on scientific evidence; face validity – PQIs are assessed by experts in the field and accepted as relevant and useful; feasibility – PQIs are measurable in commonly available datasets using data from routine practice; and predictive validity – higher quality of PQIs is associated with better patient outcomes).



Discussions during the *Prescribing Quality Indicators* session

Further, Grigory spoke about data-related issues that a researcher might face (data quality and case mix, required sample size, linkage to other data, comparability). He also discussed the evaluation of PQI implementation focusing on the relevance, actionability as well as the unintended effects of PQI implementation.

Anke Lambooj concluded the session with a presentation on *Prescribing Quality Indicators in Practice* about the types of indicators used in monitoring of prescription behaviour of general practitioners (this initiative is referred to as the *Prescription Behaviour Monitor*) and practical uses of these indicators.

*The Prescription Behaviour Monitor* includes the following indicators: volume indicators, preferred medications (preferred drugs are identified by guidelines and/or generic availability), preventive medication (including treatment indicated because of comedications or comorbidity). Anke spoke about the use of *the Monitor* in improving the quality of prescribing both internally (e.g., in Pharmacotherapy Audit meetings) and externally (rewarding systems by healthcare insurance companies) and also discussed the pros and cons of this initiative.

## **Visualization of drug utilization data**

Chaired by Ria Benkó, this session was about the role and opportunities of basic and interactive data visualization, fundamentals for selecting the optimal type of diagram, and meaningful data presentation.

Maria Matuz, in her presentation *Fundamentals of Graphical Representation*, spoke about the most important chart types used in drug utilization research. After a short history and definitions she mentioned the two main goals of visualization: exploring data and communicating results. She continued with presenting variables types, listing drug utilization variables and showing the most important graph types for categorical and for numerical data. She discussed the pros and cons of certain graphs, their role in drug utilization and as illustrations of basic statistical methods. She also discussed the visualization of trends and presented special diagram types (Lorenz curve, Pareto plot) used in drug utilization research.

Ria Benkó gave a lecture on *Graphical Considerations of Data Visualization: Demonstration through Drug Utilization Examples* in which she described common problems of data presentation in scientific literature. She provided five example figures from recently

published drug utilization studies and by a step-by-step approach amended these figures and finally came up with alternative solutions that facilitated data interpretation for readers. She closed her presentation with mentioning general principles of graphical displays and some practical hints.

Mikael Hoffmann spoke about *Interactive Visualization of Data*. After a short historical background he discussed strengths and possibilities of interactive visualization compared to static figures/graphs. Afterwards the most well-known and easily accessible interactive visualization tool, the Gapminder (or Google Motion Chart) with animated bubble graphs was presented with drug utilization-related examples for time and geospatial visualization. Mikael concluded his presentation by guiding the audience through the basic features of interactive visualization tools (zooming, brushing and filtering data).

### **Advanced educational sessions**

Four advanced sessions focused on methods used in drug utilization research, including study designs and statistical methods (with particular focus on interrupted time series and multilevel modeling).

### **Methods for assessing drug utilization and outcomes in longitudinal databases**

Morten Andersen spoke about *Measuring Drug Use in Dynamic Cohorts*. He illustrated what information can be derived from the aggregate and individual level drug utilization data and explained how these data can be analyzed using examples of a longitudinal study of inhaled corticosteroids use in asthmatics, a study of the influence of conducting a clinical trial on general practitioners' prescribing, as well as a dynamic pharmacoepidemiologic model of drug use.

Helga Gardarsdottir, in her presentation *Cohort Studies of Drug Use*, spoke about inception cohorts and treatment episodes. Inception cohorts comprise individuals at a specific risk of a disease based on some factor (e.g., time without use of the studied drug). Construction of a treatment episode – a period of subsequently prescribed or dispensed prescriptions that belong to the same time frame – requires identifying the length of medication gap and dealing with treatment overlap. Helga then spoke about the differences between prescribing data and dispensing data and gave advice around conducting database cohort studies.

Eric van Ganse, in his presentation *Use of Therapy and Outcomes: the Case of Asthma*, spoke about measuring drug exposure in asthma patients focusing on adherence and persistence. He illustrated how to define and measure outcomes (control, lung function, exacerbations as well as healthcare utilization and costs) in asthma patients. Eric concluded his presentation with demonstrating how to use longitudinal databases in drug utilization research based on examples from the ASTROLAB (*Assessment of the Safety in LABAs in Asthma in Routine Care by Combining Healthcare Databases and Direct Patient Follow Up*) study.

### **Measuring patient adherence**

Bernard Vrijens gave a lecture on the *Taxonomy of Adherence Research and Electronic Monitoring of Patient Adherence*. He described the process by which patients take their medications as prescribed in three steps: initiating therapy, implementing dose regimen and persisting on treatment. In non-adherence, something goes wrong in one or more of these three steps.

Bernard also explained that data misinterpretation can occur when adherence is estimated as a percentage and advised not to

report adherence as a percentage since it can be misleading.

Another point was that non-adherence can be divided into intentional and unintentional, and that it is important to take both into account when measuring adherence. Education to increase knowledge, motivation and measures to increase awareness were presented as three important factors influencing patient behavior.

Monique Elseviers, in her presentation on *Questioning Patient Adherence*, stated that adherence is a neglected field in drug utilization research with limited interest in specific methodology and limited awareness in drug utilization research applications. Monique described methods that are used in field research to assess non-adherence including drug concentrations, pill count, self-report and electronic monitoring. Drug concentration is an objective measure, but it can be expensive and labor intensive as well as burdensome for the patient. Pill count is simpler, but often gives spurious results due to pill dumping. Both methods have limited applicability for routine practice. Self-report can be done in various ways, for example, by interviewing the patient or the caregiver, or by using a patient diary. It is easy and cheap, but the

information is subjective and social desirability can disturb the results. Monique also spoke about the dimensions of adherence (as defined by the WHO) that include healthcare system related (e.g., relationship with provider), condition-related (e.g., presence of symptoms), patient-related (e.g., gender differences), therapy related (e.g., duration of treatment) and social/economic factors related (e.g., social support) aspects. Monique also spoke about the impact of interventions to improve adherence and pointed out that successful interventions are patient-centered, multi-faceted and conducted by a multi-disciplinary team.

Jaco Voorham concluded the session with a lecture about *Database Research on Patient Adherence*. He began by pointing out the importance of remembering that most secondary data sources used in research contain data that are collected for purposes other than research. It is convenient to use these data, and data are available for long time-periods. However, it is a limitation that the researcher can only see what is intended (prescribing), given (dispensing) or paid for (reimbursement data). There are many pitfalls when converting these data into measures of adherence.

Interpretation of patterns can be tricky and many underlying assumptions are made. To begin with, it is assumed that medication records are accurate and that medication is taken as prescribed. Other examples of assumptions are that lack of a refill means that medication is not consumed during that period, and that duplicate prescriptions are stockpiled. When pre-processing data one must decide how to handle, for example, missing data, overlapping prescriptions and false gaps. They can be handled with corrections, removals and/or imputation. Jaco concluded by stating the importance of knowing the data and thinking carefully about the choice of statistic and data pre-processing.

### **Statistical methods for multilevel and longitudinal analysis of drug utilization**

Chaired by Morten Andersen, the session was designed for researchers interested in the statistical methods used in drug utilization studies.

Juan Merlo, in his lecture called *Conceptual Introduction to Multilevel Analysis of Prescribing and Drug Use*, explained how to recognize the presence or absence of multilevel structures and guided the audience through examples of multilevel regression analysis. Multilevel regression

analysis is a relatively new statistical technique for the analysis of data with a multilevel structure. It is suitable to studying outcomes that are correlated because of the existence of multilevel structures. Examples of clusters are hospitals, wards, healthcare centers and neighborhoods. Juan explained that when one investigates clusters it is necessary to consider that individuals may be correlated within each cluster. Therefore, a correction of the intra-cluster correlation, to obtain a real statistical sample, is necessary for estimations of uncertainty. Juan presented multiple examples of drug utilization studies to facilitate the understanding of the subject.

Doug Steinke spoke about *Interrupted Time Series Analysis*. Interrupted time series analysis is

used to measure treatment effect or impact of intervention. Doug highlighted that to conduct interrupted time series analyses, a sufficient number of points before and after the intervention as well as a sufficient number of observations at each point are required. Secondary data sources such as administrative healthcare databases are often used in interrupted time series analyses. Doug then illustrated how segmented regression analyses are performed in drug utilization studies.

#### **Assessing and explaining variability in drug utilization**

Chaired by Morten Andersen, the session presented an overview of factors leading to variability in drug utilization and provided a framework for the analysis and interpretation of variability in drug use.



Discussions during the *Assessing and Explaining Variability in Drug Utilization* session

Judith de Jong, in her presentation *Explaining Medical Practice Variation – Institutional Mechanisms*, spoke about factors contributing to variations in medical practice between (groups of) physicians. Judith introduced and explained three institutional mechanisms: the regulative (rules and regulations), the normative (professional norms) and the cultural cognitive mechanism (framework physicians use in their decision-making) that influence medical practice. She also discussed the impact of innovation (“no variation without innovation”), guidelines as well as adherence to guidelines, and decision support systems on variations.

Brian Godman gave a lecture on *Policies and Cross-National Variability in Drug Use* in which he described how various health policies can influence drug utilization across countries and emphasized the importance of interpreting observed drug use variations in light of implemented health policies and interventions. Brian illustrated that such studies can help identify effective reforms that facilitate rational drug use. Further, he demonstrated how demand side initiatives could be classified under the 4 Es: Education (e.g., academic detailing, benchmarking and formularies), Economics (e.g.,

financial incentives for physicians, pharmacists or patients), Engineering (e.g., prescribing targets) and Enforcement (e.g., prescribing restrictions) supporting his presentation by multiple examples of cross-national comparisons of drug utilization across Europe.

Fanny Jansen spoke about *New Approaches for Modelling Population Level Drug Use with Demographic and Geographic Techniques*. She showed examples of geographic variation in drug use identified in studies from the US, Spain, Australia and Taiwan and also discussed demographic determinants of drug use with an emphasis on birth cohort effects (birth cohorts can have distinctive cultural and moral values and thus have different drug utilization patterns). Then, she explained the principles of modeling population level drug use with demographic (age-period-cohort analysis) and geographic approaches (spatial analysis) and explained the added value of this approach (improved description and explanation of drug utilization trends and ability to localize and target the areas at risk and in need for health interventions).

All sessions were well attended and received great feedback from participants.

## Summary of the scientific program

The scientific program of the conference included two plenary sessions, oral and poster presentations and three interactive workshops.

### Plenary session: Europe's role in the globalization of drug utilization research

Aukje Mantel-Teeuwisse, in her keynote lecture *Priority Medicines – Global Challenges in Drug Therapy and Innovation*, spoke about the WHO report entitled *Priority Medicines for Europe and the World 2013 Update*.

Objectives of this report were to provide methodology for identifying pharmaceutical 'gaps' from a public health perspective for Europe and globally, to identify opportunities for innovation to address these gaps,

and to provide a public health based pharmaceutical R&D agenda. When summarizing the priority needs, Aukje highlighted that existing drugs and existing data should be used better. For example, for expensive drugs it is important to identify patients who will benefit most (e.g., through genetic testing). Furthermore, the use of medications in children as well as in older adults and differences between men and women should be investigated. Also, a regulatory reform was suggested in which the licensing procedure is divided in two steps starting with an initial license and then, once additional studies including both clinical trials and observational studies have been conducted, the drug may receive a full license.



Participants attending the *Scientific Program*

Lastly, Aukje suggested everyone to take note of the *Priority Medicines* report and see how one could contribute to addressing the existing and emerging knowledge gaps.

Björn Wettermark, in his keynote presentation *Drug Utilization Research – a Solution for the Future*, also spoke about the content of the *Priority Medicines* report. He gave a historical overview of milestones in drug utilization research and its areas of inquiry including the aspects and consequences of drug utilization to be explored that were outlined by Dukes in 1993. Björn pointed out that the issues addressed by drug utilization research changed little over the past 20 years.

Björn referred to the WHO *Global Burden of Disease: 2004 Update* report that outlined that cardiovascular diseases are a major problem both in Europe and globally and that infections and mental illness also are common issues. These three disease areas are often studied in cross-national comparisons of drug utilization, as was found in a literature review by Gillström and Wettermark completed for the EuroDURG meeting in Antwerp in 2011.

Although there are many studies addressing the problems



**Björn Wettermark**

highlighted in the WHO report, most studies conducted so far have been descriptive thus analyses exploring underlying causes as well as studies evaluating the effectiveness of interventions are much needed.

Speaking of the future of drug utilization research, Björn highlighted that for conducting drug utilization studies solid scientific and methodological training, access to high quality data and, importantly, collaboration across specialties and countries as well as wisdom are essential.

### **Adherence to medication**

The session started with a lecture by Bernard Vrijens on *Assessment of Adherence to Medication: Strengths and Limitations of*

*Database Research Versus Electronic Monitoring.*

Bernard gave examples from research papers illustrating the issues in medication adherence (some patients do not initiate medications, some do not implement as prescribed, some do not persist). Then, Bernard discussed how adherence measurement methods vary in reliability (biased vs. reliable) and sample size (sparse vs. rich) and gave a comprehensive overview of assessment methods (direct methods, pharmacokinetics/ pharmacodynamics; self-report; pill counts; prescription and refill databases; electronic monitoring) of adherence (including initiation, implementation and persistence) in ambulatory patients.

The session also included four oral presentations covering subjects such as studying primary nonadherence using prescribing and dispensing data (*Primary Nonadherence to Statins and Antidepressants in Iceland* by Anna Birna Almarsdottir), employing econometric panel data modeling methodology to identify factors influencing adherence (*Modelling Adherence to Inhaled Corticosteroids in Patients with Asthma Using Primary Care Clinical and Prescribing Data* by Amelia Taylor), developing counselling tools to improve adherence (A

*Practical Counselling Tool to Improve Medication Adherence* by Yoleen van Camp), and understanding the perspectives of adolescents on medication adherence using online focus groups (*Towards Effective Adherence Enhancing Interventions in Asthmatic Adolescents: Results from Online Focus Groups* by Ellen Koster).



Monique Elseviers

**Drug utilization research as a tool for health policy**

Simon Hurding of the Scottish Government provided examples illustrating the role of drug utilization research in health policy in his lecture *Drug Utilisation Influencing Policy*. Simon spoke about HEAT targets (Health Improvement for the People of Scotland; Efficiency and

Governance Improvements; Access to Services; and Treatment Appropriate to Individuals) that included reducing the rate of clostridium difficile infection in hospitals by at least 30% by 2011; National Therapeutic Indicators (NTIs), Medicines Management Domains in the Quality Outcomes Framework (QOF), general practice audit requirements, Audit Scotland, and the Scottish Reduction in Antimicrobial Prescribing (ScRAP) Programme.

There were four oral presentations illustrating the interaction of drug utilization research and health policy in Europe, South America and Australia: a survey of pharmaceutical policies implemented in Europe since 2010 (*Monitoring of Pharmaceutical Policy Measures in European Countries as Tool for Health Policy* by Sabine Vogler), development and testing of a model for projecting NHS pharmaceutical expenditure (*Projecting Expenditure on Medicines in the UK NHS* by Jorge Mestre-Ferrandiz), a study of federal purchases of unlicensed medicines in Brazil from 2004 to 2012 (*Federal Procurement of Unlicensed Medicines in Brazil* by Claudia Osorio-de-Castro) and an evaluation of an Australian program implemented to improve cardiovascular health outcomes

(*Judicious Use of Cholesterol Lowering Medicines: Influencing Primary Care* by Aine Heaney).

## Drug use in hospitals

Thomas Cars summarized the challenges in conducting research on drugs used in hospitals and shared his own experiences of working with hospital drugs in his lecture *Drug Utilization in Hospitals – Perspectives and Challenges*. Thomas pointed out that, given the increasing share of specialist drugs in the R&D pipeline, there is a growing need of drug utilization data at individual level in hospitals to evaluate the rational use of hospital drugs. Thomas also illustrated how complex hospital data can be and mentioned the currently existing barriers for creating population level hospital drug utilization databases that collect information at the individual level. Thomas also spoke about the Swedish National Pharmaceutical Strategy that includes an aim to create a national database with individual level data on all medicines administered in the hospital setting. Thomas spoke of data extractions from hospital-based EHRs in Sweden and the challenges he encountered in his work, including the wide variety of EHRs systems used, hybrid state of health records including

coexisting paper and electronic documentation of administered drugs, as well as a variety of technical issues that need to be addressed at the national level.

The oral presentations that followed provided examples of drug utilization studies of hospital drugs, including the use of Portuguese INFARMED data to study biologics utilization patterns across regions (*Regional Differences in Utilisation of Biologics In Portugal* by Patrick Souverein), evaluation of the association between potentially inappropriate medications and in-hospital falls in a German geriatric teaching hospital using health records data (*Potentially Inappropriate Medication and In-Hospital Falls* by Lilli Neumann), the use of the Critical Incident Technique in studying the causes of medication administration errors made by nursing staff (*What Are the Causes of Intravenous Medication Administration Errors in Hospitals? A Critical Incident Study* by Richard Keers), as well as the results from a systematic literature review on the impact of clinical pharmacy interventions (*Economic Evaluations of Clinical Pharmacist Interventions on Hospital Inpatients: A Systematic Review 2008–2012* by James Gallagher).

## Comparison of drug use across nations

Robert Vander Stichele opened the session with a lecture on *Promises and Pitfalls of Cross-National Comparisons (CNC) of Drug Utilisation*, which he began by bringing attention to the important questions in any cross-national comparison:

1. What is compared,
2. With what purpose,
3. From which perspective,
4. With what validity, and
5. With what method?

Robert then spoke about the checklist for cross-national comparisons, used in the European Surveillance of Antimicrobial Consumption (ESAC) project. Three types of bias were described in the checklist: bias by population coverage, bias by drug



Robert Vander Stichele

coverage and bias by ambulatory care/hospital mix.

Next, an overview of previous and current attempts at cross-national comparisons was given and activities to facilitate the collection of valid national drug utilization data suitable for cross-national comparison were outlined.

The oral presentations included a comparison of the uptake of new anti-diabetic drugs in light of implemented pharmaceutical policies in France, Germany, United Kingdom and Australia using IMS Health and Australian reimbursement data (*The Diffusion of New Anti-Diabetic Drugs: an International Comparison and Its Implications* by Catherine Sermet), a systematic literature review of Latin American cross-national comparison studies with a focus on data sources and methodology used (*Systematic Review of Cross-National Drug Utilization Studies in Latin America* by Carlos Durán), comparison of utilization and adherence to pharmacotherapy following hip fracture in the US, South Korea and Spain (*Use of Pharmacologic Agents for the Secondary Prevention of Osteoporotic Fracture: A Cross-National Study* by Gabriel Sanfélix-Gimeno), as well as a study based on EHRs data from seven European regions/countries on

antiepileptic drug use in pregnant women (*Antiepileptic Drug Use Before, During and After Pregnancy: a Study in 7 European Regions* by Rachel Charlton).

## Trend and cohort studies

The session included six presentations, selected from submitted abstracts, illustrating how different study designs and methodologies can be successfully employed in answering drug utilization research questions.

Four of the cohort studies presented used the incident user design (*Economic Consequences of Contemporary Trends in Initiation of Antidepressant Therapy* by Eimir Hurley; *The Diane-35 Pill in Dutch General Practice: Large Variation in Prescribing Patterns* by Liset van Dijk; *Course and Outcome of Clozapine Treatment in Patients with Schizophrenia in Denmark* by Christiane Gasse; *Persistence to Antihypertensive Drug Class in 5225 Patients in Primary Healthcare: the Swedish Primary Care Cardiovascular Database* by Miriam Qvarnström).

Ana Afonso shared the results of a methodological study using a common protocol for analyses of two EHR-based research databases (*Association between Inhaled Long-Acting Beta-2-Agonists and the Risk of Acute Myocardial Infarction: a*

*Methodological Comparison of Two Databases*) and Cécile Billionnet presented an algorithm for identifying the indication of interest using secondary data (*Identifying Atrial Fibrillation in Patients Initiating New Oral Anticoagulants Using the French National Health Insurance Database*).

### **Drug utilization in older adults**

Debra Rowett opened the session with a presentation on *Drug Utilisation Informing Clinical Decision Making in the Elderly*. Debra highlighted that drug utilization research greatly contributed to improved utilization of medicines and also provided a number of examples of how drug utilization studies had

been employed in Australia to facilitate the rational use of medicines in older patients.

Debra also addressed the issue of polypharmacy in older individuals and spoke about the benefits of stopping medicines in older adults. This minimizes the risk for adverse drug reactions and drug interactions; it has a potential to reduce the burden of medicine management for patients, their carers and health service, and it can also lead to improved quality of life and function.

Oral presentations included a cross-national comparison study (*Cross-National Comparison of Prescribing Patterns in Australian and Dutch Nursing Homes* by Katja Taxis), an assessment of utility of the START/STOPP criteria



Lisa Pont presenting at the *Drug Utilization in Older Adults* session

in evaluating the appropriateness of prescribing based on aggregate level data (*Use of START/ STOPP Criteria to Assess Appropriate Prescribing in Older Patients with Polypharmacy in Primary Care at an Aggregated Level* by Katinka Nauta), a demonstration of a web-based tool for monitoring prescribing (*Decreasing Utilization of Propiomazine and Tramadol Among Elderly – An Illustration of a Web-Based Tool to Monitor Drug Prescribing* by Elin Dahlén) and a study of drug utilization patterns at the end of life (*Changes in Medication Use at the End of Life* by Lisa Pont).

### **Drug utilization in children and pregnant women**

Antje Neubert began the session by discussing the opportunities and challenges of studying drug use in children. The session's oral presentations included a cross-national study of medication use in pregnancy (*The Multinational Study on Medication Use in Pregnancy – Current Findings and Future Research Possibilities* by Hedvig Nordeng), presentation of results from the PROTECT project on the utilization and off-label use of long-acting beta-2-adrenoceptor agonists and anticholinergic drugs in German paediatric patients (*Long-Acting Beta-2-Adrenoceptor Agonists and Anticholinergic Drugs: Drug*

*Utilisation and Off-Label Use in Paediatric Patients Living in Bavaria* by Marietta Rottenkolber), studies of off-label use and polypharmacy in children (*Incidence of Polypharmacy in Children in Germany* by Gisbert Selke), as well as a study of anxiolytics and hypnotics use in pregnancy and outcomes in children (*Prenatal Exposure to Anxiolytics and Hypnotics and Language Competence at Three Years of Age* by Ingvild Odsbu).

### **Drug utilization and pharmacovigilance**

The session included two lectures: *Drug Use and Signal Detection in Pharmacovigilance* by Ugo Moretti and *Key Results from the ARITMO Project* by Miriam Sturkenboom.

Ugo Moretti provided a thorough overview on the subject of drug use and signal detection in pharmacovigilance and concluded that drug utilization data are essential to pharmacovigilance, not only in signal detection but also in signal prioritization and validation. Drug utilization data can also support regulatory decisions and can be used to evaluate the impact of signal communication in clinical practice.

Miriam then gave an overview of the ARITMO project and demonstrated how experimental

pharmacodynamics data, national and international pharmacovigilance databases, and clinical (e.g., EHRs) and administrative (e.g., pharmacy dispensing or reimbursement data) secondary data sources and primary data from field studies as well as literature-based evidence synthesis are used to answer the project objectives. Miriam summarized her presentation by saying that ARITMO collected many drug related factors for the arrhythmogenic potential of 588 drugs from different sources and that all data are now separately available and being interpreted. The integrated evidence allows for better regulatory and clinical decision-making and the established infrastructure may be used to look at other drugs. These lectures were followed by two oral presentations: a cross-national comparison of antipsychotics with torsadogenic liability in five European countries (*Prescribing Pattern of Antipsychotic Drugs with Torsadogenic Liability during the Years 1996–2010: the ARITMO Project* by Gianluca Trifirò) and a review of all Direct Healthcare Professional Communications issued in the European Union to assess the feasibility of evaluating the effectiveness of DHPCs using

secondary data (*Direct Healthcare Professional Communication – Can Their Effectiveness be Measured?* by Taco Monster).



Flora Haaijer-Ruskamp and Anna Birna Almarsdottir chairing the *Patient Perspective on Adverse Drug Reactions* workshop

## Interactive workshops

The meeting also included three workshops. In the *Evaluating Impact of Interventions* workshop, participants were asked to design an intervention study to evaluate impact of a national policy, using the case of regulatory warnings. The *Patient Perspective on Adverse Drug Reactions* workshop focused on patients' role in identifying adverse drug reactions; the workshop participants discussed questions around incorporating the patients' voice in medication safety decision-making. Finally, the *Drug Utilisation Research in*

*the Introduction of New Drugs* workshop included presentations from three countries (Italy, Spain, the Netherlands) that have implemented patient registries, conditional reimbursement schemes or physician incentive

schemes for the utilization of new drugs. The presentations were followed by discussions around key criteria to consider when monitoring utilization patterns for new drugs post launch.



Discussions during the *Drug Utilisation Research in the Introduction of New Drugs* workshop

**Plenary session: Challenges and opportunities for future drug utilization research: perspectives of the policymakers, healthcare providers and patients**

The aim of this concluding session of the ISPE–EuroDURG 2014 conference was to put the finger on an ever-moving future, and identify challenges and opportunities for future drug utilization research. Expectations from the past were confronted with the reality of today and

discussed from various perspectives.

Robert Vander Stichele began the session by referring to the *Scenario Analysis of the Future of Medicines* paper published in 1994 by Bert Leufkens, Flora Haaijer-Ruskamp, Albert Bakker and Graham Dukes in the British Medical Journal. Four plausible scenarios for the future were outlined in 1994:

1. Sobriety in sufficiency,
2. Risk avoidance,
3. Technology on demand,
4. Free market unfettered.

The keynote speakers were then asked to offer their perspectives on the future of the drug utilization research.

Bert Leufkens shared the (policy-maker) regulatory viewpoint on the future of drug utilization research. In his first reflections Bert stated that the four scenarios were still plausible stories on the future of medicines and that levels of ‘control and regulation’ and ‘technology embrace’ remained critical factors. He also pointed out the challenges of evidence building in orphan drug development.

With regards to the future scenario drivers, Bert mentioned the following:

1. Nature of output of pharmaceutical R&D,
2. Validity/quality of methods for quantification of disease, exposures and outcomes, and
3. How society handles new therapeutic options.

Frank May presented the perspective of a healthcare provider. Speaking of the past 20 years, Frank said that there had been few major changes in foundational healthcare systems and structures and in attitudes regarding risk-taking in healthcare: these had been key elements in the 1994 scenario analysis.



**Bert Leufkens**

However, changes in technology had been rapid and profound. Technology change had created opportunities to deterministically systematize healthcare practices and to facilitate information creation, dissemination and communication aimed at both healthcare professionals and the public. However, he warned of inherent hazards in this rush to systematize healthcare.

Frank also spoke of substantial achievements in drug utilization research over the past 20 years. With regards to future challenges and opportunities, Frank pointed out that more incisive research was needed in a number of key areas: patients’ decisions about adherence/persistence with prescribed therapies (e.g., factors motivating patients’ adherence); prescribers’ decisions about

judiciousness of therapy (e.g., prescribing quality indicators); and how prescriber decision-making can be reliably enhanced (e.g., interventions for enhancing clinical care).



**Frank May**

Nicky Britten concluded the session speaking about the patient perspective. Nicky said that, given that patients are the end users of drugs, drug utilization research should pay greater attention to them and offered two approaches for achieving this: having patients as the focus of drug utilization research (this would help identify topics important to patients and bring attention to real life problems) and involving patients as partners in drug utilization research (i.e., *Patient and Public Involvement in Research, PPI*). Nicky then explained what PPI is and shared her experiences of working with patients as partners in drug utilization research. Nicky

also outlined the challenges (e.g., time-consuming and emotionally demanding, hostile attitudes of researchers and clinicians, lack of sufficient funding) and opportunities (e.g., research which is more likely to be implemented, reduced research wastage, increasing patients' understanding of evidence-based medicine) of having patients as partners in research.



**Nicky Britten**

Nicky mentioned the following among the possible future scenarios of drug utilization research:

1. Broader view of how patients use medicines in their everyday lives, going beyond adherence,
2. Collaboration with social and behavioral scientists, and
3. Normalization of Patient and Public Involvement in drug utilization research.

## Farewell symposium Flora Haaijer-Ruskamp

On the final day of the ISPE–EuroDURG 2014 conference, the remarkable career of Flora Haaijer-Ruskamp, Professor in Drug Utilisation Studies at the University of Groningen, was celebrated. Fellow colleagues, friends and family joined Flora in a symposium to mark the occasion of her retirement and to honor her contribution to drug utilization research.

The dedicated symposium, chaired by Dick de Zeeuw, included lectures from Robert Vander Stichele, Bert Leufkens, Niek Klazinga, Petra Denig and, of course, Flora herself, highlighting the width and depth of her research during the years.

Professor Flora Haaijer-Ruskamp received her master's degree in medical sociology in 1976 and defended her doctoral thesis on studies elucidating the variation in prescribing patterns of physicians in 1984. She was one of the first in this field who studied multivariate relationships, looking at practice, practitioner and patient characteristics.

Since 1994 she has held the first chair in Drug Utilisation Studies at the Department of Clinical Pharmacology, University of Groningen, the Netherlands.



**Flora Haaijer-Ruskamp**

Professor Flora Haaijer-Ruskamp's research has focused on rational drug use – specifically on the development and evaluation of strategies and interventions to optimize drug treatment, taking into consideration social, cultural and behavioral aspects.

In the growing field of drug utilization studies and pharmacoepidemiology, her team has collaborated widely both nationally and internationally. Flora has been involved in a number of international projects, including the European Drug Education Programme (DEP), YEMDAP in Yemen and the SAR (Self-medication with Antibiotics and Resistance) study. Over the years, she has published widely in

peer-reviewed journals, contributed to book chapters and books, in addition to having supervised over 20 PhD students.

Professor Flora Haijjer-Ruskamp has also played a pivotal role in

the advance of EuroDURG, having served as chair of the society since its inaugural meeting at Lake Balaton in 1996 up until 2004.



Farewell lecture by Flora Haijjer-Ruskamp



The audience showing their appreciation



## Special initiatives – OECD session

A special session on prescribing quality indicators was jointly arranged by EuroDURG and Niek Klazinga, coordinator of the OECD Health Care Quality Indicator program. A selected number of data holders and academic researchers received a special invitation to discuss prescribing quality indicators selected for inclusion in the OECD Health Care Quality Indicator program.

During the meeting, the OECD country representatives were asked to provide data for three sets of indicators for primary care.

### *Antibiotics use*

- 1a. Overall volume of antibiotics for systemic use
- 1b. Volume of cephalosporin and quinolones as a proportion of all antibiotics prescribed

### *Treatment of diabetes*

- 2a. Use of cholesterol lowering treatment in diabetic patients
- 2b. Use of recommended antihypertensives in diabetic patients

### *Medication safety (use of benzodiazepines in older adults)*

- 3a. Chronic use of benzodiazepines in adults older than 65 years
- 3b. Use of long-acting benzodiazepines in adults older than 65 years

The session included an active discussion on the possibilities and pitfalls of international comparisons with the selected indicators. Future similar networking activities around prescribing quality indicators were requested.



Niek Klazinga

## Award winners

The conference featured over 300 abstracts covering a wide spectrum of drug utilization research questions, including drug utilization in specific therapeutic areas (infectious diseases, respiratory diseases, cardiovascular diseases and diabetes, psychotropics and pain medications, oncologicals and biologicals), drug utilization in specific populations (pregnant women, children and older adults), drug utilization in ambulatory care and in hospitals, medication adherence, pharmacovigilance, pharmaco-economics and health policy.

Nine interactive poster walks were organized for all attendees and poster presentations were evaluated by two judges (a EuroDURG board member chairing the walk and an invited external judge). The following researchers were recognized for the quality of both their research and presentation.

### *Cardiovascular diseases and diabetes*

Doti P. Martono et al. University of Groningen, the Netherlands  
Predictors of treatment response in initial users of metformin and sulfonylurea derivatives: a systematic review

### *Psychotropics/pain medication*

Joëlle Hoebert et al. Utrecht Institute for Pharmaceutical Sciences, the Netherlands  
Variability in market uptake of psychotropic medicines in Europe reflects cultural diversity

### *Antibacterials/Oncologicals/Biologicals*

Yaser Bazargani et al. Utrecht University, the Netherlands  
Endocrine therapy for breast cancer patients in a middle-income country (South Africa)

### *Medication adherence*

Alison Wright et al. University of Manchester, United Kingdom  
Adherence to first-line antidiabetic medication in newly diagnosed type 2 diabetes: retrospective analysis of the Clinical Practice Research Datalink

### *Drug utilization in children and pregnant women*

Carmen D'Amore et al. National Institute of Health, Rome, Italy  
Patterns of antihypertensive medication use during pregnancy: a population-based study

*Drug utilization in older adults*

Jojanneke van Summeren et al. University of Groningen, the Netherlands  
Medication review in elderly patients with polypharmacy: effects of the use of a tool to RAnk Patient Preferences (RAPP)

*Drug utilization research and pharmacovigilance*

Mona Vestergaard Laursen et al. Danish Health and Medicines Authority, Denmark

Drug utilisation studies as a tool for regulatory drug safety surveillance

*Drug utilization research and health policy*

Elien Van Bever. Ghent University, Belgium

50 Shades of prescriptions: diversity of prescribing regulations in Europe

*Breadth and depth of drug utilization research*

Patrick Souverein et al. Utrecht University, the Netherlands

(Non)availability of dosage instructions in electronic health care databases and exposure (mis)classification: the example of antidepressants

Special thanks to Janet Krska, Peter Mol, Katja Taxis, Lisa Pont, Anna Birna Almarsdottir, Eric van Ganse, Morten Andersen, Ria Benkő, Vera Vlahović-Palčevski and Marion Bennie for chairing the poster walks.

EuroDURG and Wiley awarded the winners with a copy of the upcoming book *Drug Utilization Research: Methods and Applications*.



The award winners

## Evaluation of the meeting

Participants were asked by emails sent out after the conference to evaluate the event. 164 out of 303 participants responded to the questionnaire, where ratings were coded ranging from 1 (“very poor”) to 10 (“excellent”). 89 of the respondents had never before been to a EuroDURG or ISPE conference. 56% identified themselves as working in academia; 20% as coming from healthcare administrations or authorities. Participants with a clinical or other healthcare background made up 11%, while health insurance organizations provided 4% of participants. 10% stated other fields of work, for example, research, pharmaceutical companies, non-governmental organizations, and others.

The overall ratings for various aspects of the conference are shown in Figure 1. While the social program and the value for networking were generally rated highest, they also show the greatest tendency for individually differing opinions. Scientific content and relevance for work were rated very similarly, with the latter showing a slightly greater individual spread in their evaluation.

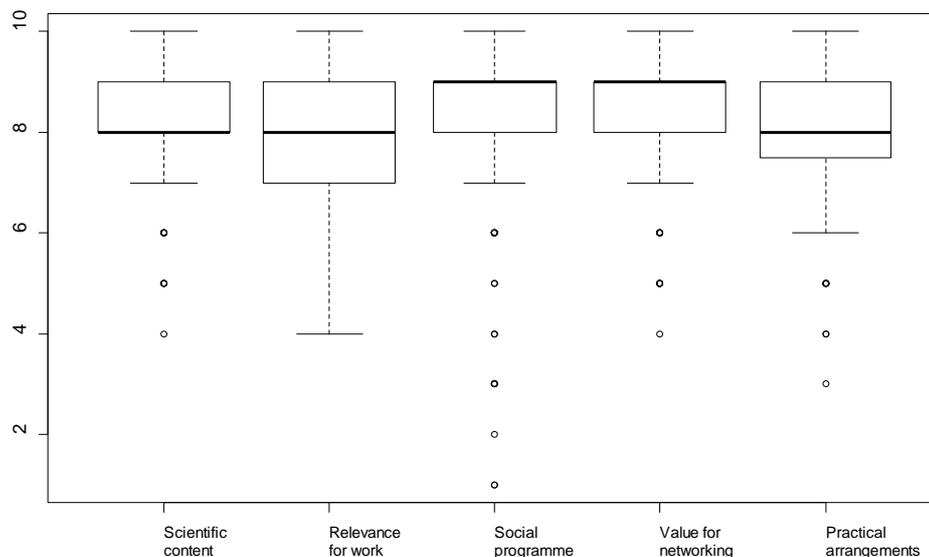
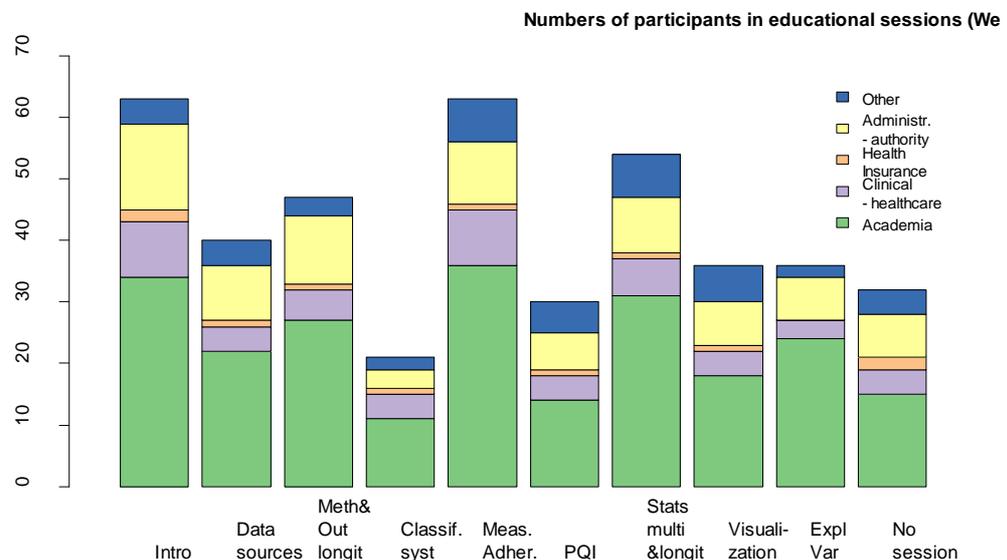


Figure 1. Overall rating of the conference

For the educational sessions on the first day, a priori attractiveness differed strongly (Figure 2). Leaving out the introductory session, the number of participants ranged from 21 for Classification Systems and Measurement Units to triple that value for Measuring Patient Adherence.

Analyses by field of work provide additional insight into the specific work-related interests. The differences also illustrate that the wide range of topics offered successfully catered for different professional needs.

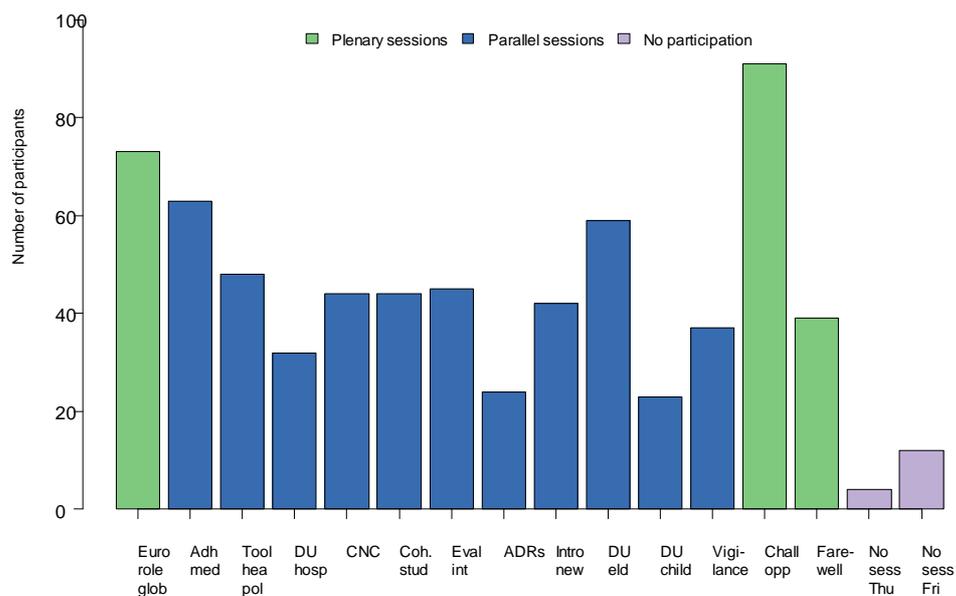


**Figure 2. Participation in the educational sessions**

Legend:

Intro	Introduction to educational sessions for drug utilization (DU) research
Data sources	Data sources for DU including quality and validity
Meth&Out longit.	Methods for assessing DU and outcomes in longitudinal datasets
Classif. Syst.	Classification systems and measurement units of drug utilization
Meas. Adher.	Measuring patient adherence
PQI	Prescribing quality indicators
Stats multi&longit	Statistical methods for multilevel and longitudinal analysis
Visualization	Visualization of DU data
Expl Var	Assessing and explaining variability in DU

Participation in the various sessions of the scientific program, both plenary lectures and track sessions, varied substantially (Figure 3). The topic of adherence to medication was the top-ranking track session by number of participants, with the one centering on older adults being the close second.

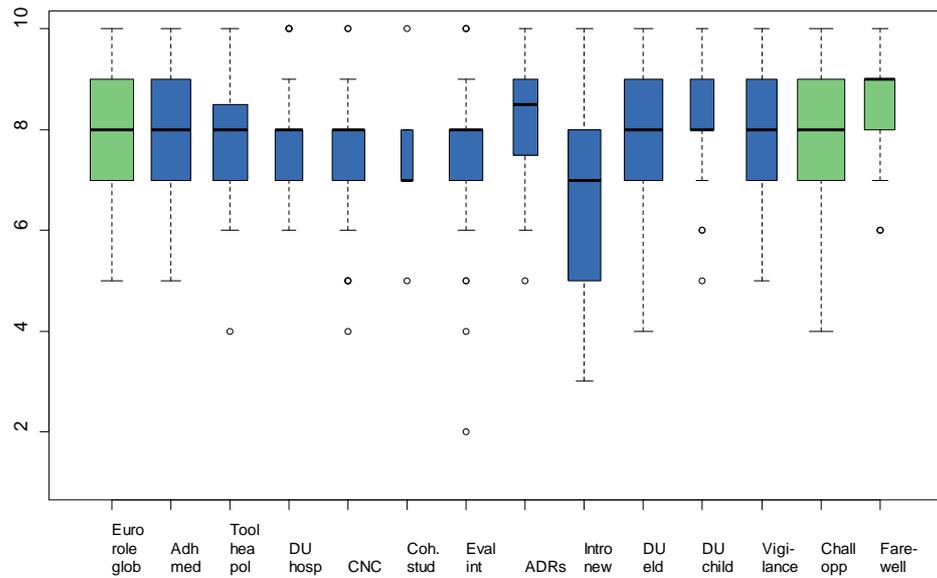


**Figure 3. Participation in the scientific sessions**

Legend:

Euro role glob	Europe’s role in the globalization of DU research
Adh med	Adherence to medication
Tool hea pol	DU as a tool for health policy
DU hosp	DU in hospitals
CNC	Cross national comparisons
Coh. stud	Trend and cohort studies
Eval int	Evaluating impact of interventions
ADRs	Patient perspective on ADRs
Intro new	DU in the introduction of new drugs
DU eld	DU in older adults
DU child	DU in children
Vigilance	DU and pharmacovigilance
Chall opp	Challenges and opportunities for future DU research
Farewell	Farewell symposium in honor of Flora Haaijer-Ruskamp

Of the plenary sessions, the event with the most personal note, the farewell symposium for Flora Haaijer-Ruskamp, scored the highest and most consistent rating (Figure 4). Otherwise, again each session received some top ratings (10 out of 10), with the median generally being around 8.



**Figure 4. Rating of the scientific sessions**

Legend: See previous figure

The questionnaire also included free-form fields to express which topics or aspects should be expanded and which could be cut down. As might be expected, there is no common theme to be found; for example, some participants expressed an interest in more coverage of adverse drug reactions, whereas in others' opinions this was already too prominent. A number of commentators expressed their view that the mix was well balanced. The most common wish was to hear more about methodological aspects.

## Appendices

### Appendix 1: Scientific program

Wednesday, 27 August, 2014

08.30- 09.00 Registration and Coffee

09.00- 09.30 Introduction to educational sessions for drug utilization research

09.30- 11.00 W1A: Björn Wettermark (chair)

*Basic educational session: Data sources for drug utilization including quality and validity*

Aim: To provide knowledge on the value of different data sources that can be used for drug utilization research, and provide insight in record linkage and validation studies.

Speakers: Tatiana Borges Luz, Irene Eriksson, Maria Rikala

09.30- 11.00 W1B: Eric van Ganse (chair)

*Advanced educational session: Methods for assessing drug utilization and outcomes in longitudinal databases*

Aim: Using examples from Electronic Health Records (EHRs) and claims data, we shall discuss characteristics of longitudinal datasets that are of direct use (e.g., age, sex, comorbidity), or that can be used as proxies in drug utilization research. Key analysis methods will be presented. Validation methods will also be mentioned, e.g., in the development of scores or algorithms.

Speakers: Morten Andersen, Helga Gardarsdottir, Eric van Ganse

11.00- 11.30 Coffee break

11.30- 13.00 W2A: Hanne Strom (chair)

*Basic educational session: Classification systems and measurement units of drug utilization*

Aim: To give an overview of classification systems for medicinal products. To describe the Anatomical Therapeutic Chemical (ATC) classification system and the unit of measurement (DDD), and how to use this methodology

Speakers: Hanne Strom, Hege Salvesen Blix, Solveig Sakshaug

- 11.30-13.00 W2B Monique Elseviers (chair)  
*Advanced educational session: Measuring patient adherence*  
Aim: To give a general introduction on how to measure patient adherence both using the methodology of field studies as well as database research.  
Speakers: Bernard Vrijens, Monique Elseviers, Jaco Voorham
- 13.00-14.00 Lunch
- 14.00-15:30 W3A Petra Denig (chair)  
*Basic educational session: Prescribing quality indicators*  
Aim: To provide knowledge and insight about definitions, taxonomy, and domains of Prescribing Quality Indicators (PQI). To provide knowledge about the development and requirements for PQI. To present recent developments and examples from practice for using PQI for different purposes.  
Speakers: Petra Denig, Grigory Sidorenkov, Anke Lambooj
- 14.00-15:30 W3B Morten Andersen (chair)  
*Advanced educational session: Statistical methods for multilevel and longitudinal analysis of drug utilization*  
Aim: To provide knowledge about statistical principles for multilevel and longitudinal analysis of drug utilization data.  
Speakers: Doug Steinke, Juan Merlo
- 15.30-16.00 Coffee break
- 16.00-17.30 W4A Ria Benkő (chair)  
*Basic educational session: Visualization of drug utilization data*  
Aim: To provide fundamentals to enable correct interpretation of visualized data/basic statistics. To understand the role and opportunities of data visualization. To enable optimal diagram type selection. To learn technical requirements of meaningful data presentation.  
Speakers: Maria Matuz, Ria Benkő, Mikael Hoffmann

- 16.00- W4B Morten Andersen (chair)  
17.30 *Advanced educational session: Assessing and explaining variability in drug utilization*  
Aim: To present an overview of factors leading to variability in drug utilization, to provide knowledge on how the variation can be assessed and to outline a framework for the analysis and interpretation of variability in drug use, possibly providing directions for future research.  
Speakers: Judith de Jong, Brian Godman, Fanny Jansen
- 18.00- Reception at the Academy Building  
19.00 This reception is offered by the University of Groningen, the Municipality of Groningen and the Province of Groningen

#### Thursday, 28 August, 2014

- 08.30- Registration and Coffee  
09.00
- 09.00- T1: Lisa Pont (Chair)  
10.00 *Plenary session: Europe's role in the globalization of drug utilization research*  
*Keynote lecture: Priority medicines – the global challenges in drug therapy and innovation*  
Aukje Mantel-Teeuwisse (the Netherlands)  
*Keynote lecture: Drug utilization research – a solution for the future*  
Björn Wettermark (Sweden)
- 10.00- Coffee break  
10.30
- 10.30- T2A: Monique Elseviers (chair)  
12.00 *Parallel session (Lecture+Abstracts): Adherence to medication*  
Aim: To show strengths and limitations of measuring patient adherence using databases and clinical studies.  
*Key lecture: Assessment of adherence to medication: strengths and limitations of database research versus electronic monitoring*  
Bernard Vrijens (Belgium)
- 10.30- Do patients initiate therapy? Primary nonadherence to  
11.00 statins and antidepressants in Iceland.  
11.15 Anna Birna Almarsdottir (Denmark)

- 11.15-11.30 Modelling adherence to inhaled corticosteroids in patients with asthma using primary care clinical and prescribing data.  
Amelia Taylor (UK)
- 11.30-11.45 A practical counselling tool to improve medication adherence.  
Yoleen van Camp (Belgium)
- 11.45-12.00 Towards effective adherence enhancing interventions in asthmatic adolescents: results from online focus groups.  
Ellen Koster (the Netherlands)
- 10.30-12.00 T2B: Marion Bennie (chair)  
*Parallel session (Lecture+Abstracts): Drug utilization as a tool for health policy*  
Aim: To demonstrate how drug utilization information and intelligence can be used to inform health policy and drive changes
- 10.30-11.00 *Key lecture: When drug utilization influences policy (in Scotland)*  
Simon Hurding (UK)
- 11.00-11.15 Monitoring of pharmaceutical policy measures in European countries as tool for health policy  
Sabine Vogler (Austria)
- 11.15-11.30 Projecting expenditure on medicines in the UK NHS  
Jorge Mestre-Ferrandiz (UK)
- 11.30-11.45 Federal procurement of unlicensed medicines in Brazil  
Claudia Osorio-de-Castro (Brazil)
- 11.45-12.00 Judicious use of cholesterol lowering medicines: influencing primary care  
Aine Heaney (Australia)
- 12.00-14.00 Lunch and poster walks, OECD lunch session
- 14.00-15.30 T3A: Vera Vlahović-Palčevski (chair)  
*Parallel session (Lecture+Abstracts): Drug use in hospitals*  
Aim: The session focuses on data availability and methods for researching, improving and evaluating the quality of hospital drug use.
- 14.00-14.30 *Key lecture: Drug utilization in hospitals – perspectives and challenges*  
Thomas Cars (Sweden)
- 14.30-14.45 Regional differences in utilisation of biologicals in Portugal  
Patrick Souverein (the Netherlands)

- 14.45-15.00 Potentially Inappropriate Medication and in-hospital falls  
Lilli Neumann (Germany)
- 15.00-15.15 What are the causes of intravenous medication administration errors in hospitals? A critical incident study  
Richard Keers (UK)
- 15.15-15.30 Economic evaluations of clinical pharmacist interventions on hospital inpatients: A systematic review 2008–2012  
James Gallagher (Ireland)
- 14.00-15.30 T3B: Robert Vander Stichele (chair)  
*Parallel session (Lecture+Abstracts): Comparison of drug use across nations*  
Aim: To provide an overview of promises and pitfalls of newer methods of cross-national comparison of drug utilization which go beyond assessment of volume or expenditure.
- 14.00-14.30 *Key lecture: Promises and pitfalls for cross-national comparisons*  
Robert Vander Stichele (Belgium)
- 14.30-14.45 The diffusion of new anti-diabetic drugs: an international comparison and its implications  
Catherine Sermet (France)
- 14.45-15.00 Systematic review of cross-national drug utilization studies in Latin America  
Carlos Durán (Belgium)
- 15.00-15.15 Use of pharmacologic agents for the secondary prevention of osteoporotic fracture: a cross-national study  
Gabriel Sanfélix-Gimeno (Spain)
- 15.15-15.30 Antiepileptic drug use before, during and after pregnancy: a study in 7 European regions  
Rachel Charlton (UK)
- 14.00-15.30 T3C: Petra Denig (chair)  
*Parallel session (Selected Top Abstracts): Trend and cohort studies*
- 14.30-14.40 Economic consequences of contemporary trends in initiation of antidepressant therapy  
Eimir Hurley (US)

- 14.40-14.50 Association between inhaled long-acting beta-2-agonists and the risk of acute myocardial infarction: a methodological comparison of two databases  
Ana Afonso (the Netherlands)
- 14.50-15.00 Identifying atrial fibrillation in patients initiating new oral anticoagulants using the French national health insurance database  
Cécile Billionnet (France)
- 15.00-15.10 The Diane-35 pill in Dutch general practice: large variation in prescribing patterns  
Liset van Dijk (the Netherlands)
- 15.10-15.20 Course and outcome of clozapine treatment in patients with schizophrenia in Denmark  
Christiane Gasse (Denmark)
- 15.20-15.30 Persistence to antihypertensive drug class in 5225 patients in primary healthcare: the Swedish primary care cardiovascular database  
Miriam Qvarnström (Sweden)
- 15.30-16.00 Coffee break
- 16.00-17.30 T4A: Peter Mol (chair)  
*Parallel session (Workshop): Evaluating impact of interventions*  
Workshop leaders: Peter Mol, Almath Spooner, Jane Ahlquist-Rastad  
Aim: To design an intervention study for evaluating the impact of a regulatory policy/warning. Participants in the workshop will have to apply their knowledge on potential study designs, suitable interventions, outcome measures and feasibility issues.
- 16.00-17.30 T4B: Anna Birna Almarsdottir (chair)  
*Parallel session (Workshop): Patient perspective on Adverse Drug Reactions (ADRs)*  
Workshop leaders: Janet Krska, Flora Haijjer-Ruskamp, Anna Birna Almarsdottir  
Aim: To increase participants' understanding of the patient perspective on ADRs and to put this knowledge to use in a practical framework of how to: (1) Involve the users of medicines in identifying new ADRs; (2) Incorporate the patient perspective in the regulatory process on medication safety; (3) Improve ADR signal detection and management at the doctor-patient encounter by including the patients' voice.

- 16.00- T4C: Brian Godman (chair), Jean-Paul Fagot (co-chair)  
 17.30 *Parallel session (Workshop): Drug utilization in the introduction of new drugs*  
 Workshop leaders: Antonia Agusti, Ad Schuurman, Entela Xoxi  
Aim: To provide guidance to health authority personnel and researchers on potential ways forward to optimize data collection and analysis surrounding drug utilization of new drugs. This can include physician incentive schemes for new drugs.
- 17.30- EuroDURG General assembly  
 18.30  
 19.30 EuroDURG party/dinner

### Friday, 29 August, 2014

- 08.00- Coffee  
 08.30
- 08.30- F1A: Katja Taxis (chair)  
 10.00 *Parallel session (Lecture+Abstracts): Drug utilization in older adults*  
Aim: To present research on deprescribing addressing issues according to different therapeutic areas and different settings
- 08.30- *Key lecture: Drug utilisation informing clinical decision making in the elderly*  
 09.00 Debra Rowett (Australia)
- 09.00- Cross-national comparison of prescribing patterns in  
 09.15 Australian and Dutch nursing homes  
 Katja Taxis (the Netherlands)
- 09.15- Use of START/ STOPP criteria to assess appropriate  
 09.30 prescribing in older patients with polypharmacy in primary care at an aggregated level  
 Katinka Nauta (the Netherlands)
- 09.30- Decreasing utilization of propiomazine and tramadol  
 09.45 among elderly – an illustration of a web-based tool to monitor drug prescribing  
 Elin Dahlén (Sweden)
- 09.45- Changes in medication use at the end of life  
 10.00 Lisa Pont (Australia)

- 08.30-10.00 F1B: Katrin Janhsen (chair)  
*Parallel session (Lecture+Abstracts): Drug utilization in children and pregnant women*  
Aim: To give an overview of drug utilization research in children, youths and pregnancy especially regarding assumed or proven drug safety and effectiveness issues.
- 08.30-09.00 *Key lecture: Drug utilisation in children – challenges and chances*  
 Antje Neubert (Germany)
- 09.00-09.15 Long-acting beta-2-adrenoceptor agonists and anticholinergic drugs: drug utilisation and off-label use in paediatric patients living in Bavaria (Germany)  
 Marietta Rottenkolber (Germany)
- 09.15-09.30 Incidence of polypharmacy in children in Germany  
 Gisbert Selke (Germany)
- 09.30-09.45 The Multinational Study on Medication Use in Pregnancy – current findings and future research possibilities  
 Hedvig Nordeng (Norway)
- 09.45-10.00 Prenatal exposure to anxiolytics and hypnotics and language competence at three years of age  
 Ingvild Odsbu (Norway)
- 08.30-10.00 F1C: Elisabetta Poluzzi (chair)  
*Parallel session (Lecture+Abstracts): Drug utilization and pharmacovigilance*  
Aim: To illustrate different methods in drug utilization data analysis, in order to give a population perspective to pharmacovigilance findings.
- 08.30-09.30 *Key lecture: Drug use and signal detection in pharmacovigilance*  
 Ugo Moretti (Italy)  
*Key lecture: Key results from the ARITMO project*  
 Miriam Sturkenboom (the Netherlands)
- 09.30-09.45 Prescribing pattern of antipsychotic drugs with torsadogenic liability during the years 1996–2010: the ARITMO project  
 Gianluca Trifirò (Italy)
- 09.45-10.00 Direct Healthcare Professional Communication – can their effectiveness be measured?  
 Taco Monster (the Netherlands)
- 10.00-11.00 Coffee break and poster walks

- 11.00-12.30 *Plenary session: Challenges and opportunities for future drug utilization research: perspectives of the policymakers, healthcare providers and patients*
- Aim: To put our finger on an ever moving future and identify challenges and opportunities for future drug utilization research. Expectations from the past will be confronted with the reality of today, and discussed from the perspective of the policy makers, healthcare providers and patients.
- Keynote lecture: The policy makers and regulators viewpoint*  
Bert Leufkens (the Netherlands)
- Keynote lecture: The healthcare providers viewpoint*  
Frank May (Australia)
- Keynote lecture: Patients will have the last word*  
Nicky Britten (UK)
- 12.30-13.00 Closing remarks
- 13.00-14.00 Packed Lunch and Coffee
- 14.00-18.00 Farewell symposium in honor of Flora Haaijer-Ruskamp including lectures and reception

## Appendix 2: Farewell symposium Flora Haaijer-Ruskamp

Program chair: Dick de Zeeuw (Clinical Pharmacy and Pharmacology, UMCG)

13.15- 14.00	Welcome with coffee in the Reception area (Fonteinpatio)
14.00- 14.15	Drug utilization research in Europe Robert Vander Stichele (Ghent University, Belgium)
14.15- 14.30	Drug utilisation and pharmaceutical policy Bert Leufkens (Utrecht University, the Netherlands)
14.30- 14.45	Prescribing quality indicators in the OECD Niek Klazinga (University of Amsterdam, the Netherlands)
14.45- 15.00	Flora's role in drug utilisation studies: past, present, and future Petra Denig (University of Groningen, the Netherlands)
15.00- 15.15	Break
15.15- 16.00	Farewell lecture Professor Flora Haaijer-Ruskamp
16.00- 16.30	Speeches
16.30- 18.00	Reception



Discussions during a coffee break